

The preferred embodiments of the present invention provide a process for the preparation of a derivative of a polymer having at least one functional group, wherein the process comprises the following step (i):

- A1

 - (i) reacting a polymer having at least one functional group, with at least one activating reagent or a derivative of an activating reagent in a homogeneous phase.

The preferred embodiments of the present invention also provide a derivative of a polymer having at least one functional group, preparable by a process which comprises the following step (i):

- B2

 - (i) reacting the polymer having at least one functional group, with at least one activating reagent or a derivative of an activating reagent in a homogeneous phase.--

Please insert the heading --Detailed Description-- on page 2, line 31.

Please insert the following paragraph immediately following the newly inserted "Detailed Description" heading:

A2

--A process which makes it possible to derivatize polymers having functional groups in a simple manner in a homogeneous phase is provided.--

Please delete the paragraphs beginning on page 2, line 32 and ending on page 2, line 39 and insert in their place the following paragraphs:

A3

--In the context of the process according to a preferred aspect of the invention, it is possible to react the polymer having at least one functional group firstly with an activating reagent in homogeneous phase.

Likewise, it is of course also possible in the process according to a preferred aspect of the invention to react the polymer having at least one functional group with a mixture of two or more suitable activating reagents. These can be reacted simultaneously with the polymer. Likewise, the two or more activating reagents can also be reacted successively with the polymer.--

Please delete the paragraph beginning on page 3, line 21 and ending on page 3, line 25 and insert in its place the following paragraph:

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--In the context of the process according to a preferred aspect of the invention, it is also possible to start from a prederivatized polymer to improve the solubility of the polymer. Here, the degree of derivatization of the prederivatized polymer and/or the nature of the derivatizing groups which the prederivatized polymer contains is/are expediently set according to the solvent or solvent mixture used, in which the prederivatized polymer is meant to be soluble.--

Please delete the paragraphs beginning on page 3, line 31 and ending on page 3, line 39 and insert in their place the following paragraphs:

--Accordingly, a preferred aspect of the present invention also relates to a process, as defined above, further comprising step (ii):

(ii) reaction of the reaction product from the polymer having at least one functional group and the activating reagent, with a derivatizing reagent.

In the context of this embodiment of the process according to a preferred aspect of the invention, the polymer having at least one functional group can be reacted simultaneously, i.e. in the sense of a "one-pot reaction" with at least one activated and/or at least one non-activated derivatizing reagent and/or an activating reagent.--

Please delete the paragraph beginning on page 4, line 5 and ending on page 4, line 14 and insert in its place the following paragraph:

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--If, as described above, a polymer is reacted with different activating reagents, these activated functional groups can have differing reactivity to one or more derivatizing reagents. Accordingly, it is possible in the context of the process according to a preferred aspect of the invention to derivatize functional groups selectively in this manner. The term "selective" in this connection means that a polymer which has, for example, two or more functional groups which are different from one another is

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reacted with, for example, two different activating reagents so that a subsequent reaction with a derivatizing reagent for derivatization takes place mainly to exclusively on the activated functional group(s) which is or are activated with one of these two activating reagents, as a rule on the functional group(s) which is/are more reactively activated with respect to the derivatizing reagent.--

Please delete the paragraphs beginning on page 4, line 31 and ending on page 4, line 38 and insert in their place the following paragraphs:

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-- In the process according to a preferred aspect of the invention, it is furthermore possible to react the activating reagent with the derivatizing reagent before the reaction with the polymer having at least one functional group in order then to react this reaction product with the polymer having at least one functional group.

A preferred aspect of the present invention therefore also relates to a process, as described above, where the derivative of the activating reagent is obtained by prior reaction of the activating reagent with a derivatizing reagent.--

Please delete the paragraph beginning on page 5, line 5 and ending on page 5, line 28 and insert in their place the following paragraphs:

A8

--It is likewise possible in the context of the process according to a preferred aspect of the invention with appropriate choice of the activating reagent and/or of the derivatizing reagent that in the reaction of the product from the reaction of activating reagent and derivatizing reagent with the polymer having at least one functional group some, or the entirety, of the structure of the activating reagent present in the reaction product of activating reagent and derivatizing reagent remains in the polymer.

A further, possible embodiment of a preferred aspect of the present invention consists in reacting the polymer having at least one functional group, with different products from reactions of activating reagents and derivatizing reagents. Thus, for example, a mixture of compounds can be reacted with the polymer, the mixture comprising reaction products of an activating reagent and two or more different derivatizing

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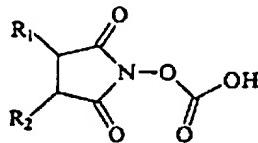
reagents. A mixture is likewise possible which comprises reaction products of a derivatizing reagent and two or more different activating reagents. Of course, it is also possible, should this be necessary, to employ a mixture which comprises reaction products of two or more different activating reagents and two or more different derivatizing reagents. Obviously, it is also possible in the context of a preferred aspect of the present invention to react the different reaction products of activating reagent and derivatizing reagent not as a mixture, but individually and in the desired sequence, with the polymer having at least one functional group.

Accordingly, a preferred aspect of the present invention also describes a process as described above, where the polymer having at least one functional group is reacted with at least two different derivatives of an activating reagent and the reactions are carried out successively with one derivative in each case.--

Please delete the paragraph beginning on page 6, line 7 and ending on page 6, line 15 and insert in its place the following paragraph:

--In particular, a preferred aspect of the present invention relates to a process, as described above, characterized in that the activating reagent is derived from a compound of the following structure (I):

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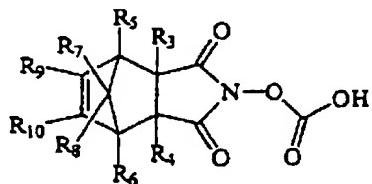
(I)

where R₁ and R₂ are identical or different and can be straight-chain, branched-chain or bridged to give a carbocycle or a heterocycle and are selected such that the activating reagent or the derivative of the activating reagent can be reacted in homogeneous phase with the polymer having at least one functional group.--

Please delete the paragraph beginning on page 6, line 20 and ending on page 6, line 31 and insert in its place the following paragraph:

--In a preferred embodiment, a preferred aspect of the present invention describes a process, as described above, which is characterized in that the activating reagent is derived from a compound of the following structure (I')

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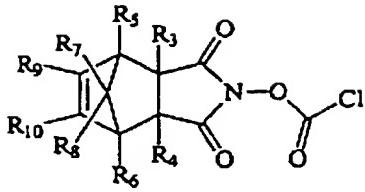
(I')

where R₃ to R₁₀ can be identical or different and can be hydrogen, straight-chain or branched-chain alkyl, aryl, cycloalkyl, heterocyclic and aralkyl radicals having up to 30 C atoms, or else a number of R₃ to R₁₀ radicals can in turn be bridged to give a carbocycle or heterocycle and are selected such that the activating reagent or the derivative of the activating reagent can be reacted in homogeneous phase, with the polymer having at least one functional group.--

Please delete the paragraph beginning on page 7, line 1 and ending on page 7, line 7 and insert in its place the following paragraph:

--A preferred aspect of the present invention further describes a process, as described above, characterized in that the activating reagent has the following structure (II)

A11



(II)

where R₃ to R₁₀ are as defined above.--

TOP SECRET - FEDERAL BUREAU OF INVESTIGATION

Please delete the paragraph beginning on page 7, line 12 and ending on page 7, line 15 and insert in its place the following paragraph:

--In a particularly preferred embodiment, a preferred aspect of the present invention describes a process, as described above, which is characterized in that the activating reagent is derived from a compound of the structure (II), as indicated above, where R₃ to R₁₀ is in each case hydrogen.--

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Please delete the paragraph beginning on page 7, line 29 and ending on page 7, line 30 and insert in its place the following paragraph:

A13

--Very generally, polymers are employed in the process according to a preferred aspect of the invention which, as at least one functional group, have a group which has at least one nucleophilic unit.--

Please delete the paragraph beginning on page 8, line 5 and ending on page 8, line 9 and insert in its place the following paragraph:

A14

--A preferred aspect of the present invention therefore also relates to a process, as described above, characterized in that the functional group of the polymer having at least one functional group is an OH group, an NHR₁₁ group, an SH group, an OSO₃H group, an SO₃H group, an OPO₃H₂ group, an OPO₃HR₁₁ group, a PO₃H₂ group, a PO₃HR₁₁ group, a COOH group or a mixture of two or more thereof.--

Please delete the paragraph beginning on page 8, line 19 and ending on page 8, line 21 and insert in its place the following paragraph:

A15

--Here, in the context of a preferred aspect of the invention the term "polymer" obviously likewise includes higher molecular weight compounds, which are designated in polymer chemistry as "oligomers".--

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Please delete the paragraph beginning on page 10, line 5 and ending on page 10, line 8 and insert in its place the following paragraphs:

A16

--In addition, it is also possible to react the activated polymer with nucleophilic chiral compounds. Examples of such chiral nucleophiles which may be mentioned are, for example:

borneol, (-)-methanol, (-)-ephedrine, α -phenylethylamine, adrenaline, dopamine.--

A17

Please delete the paragraphs beginning on page 10, line 20 and ending on page 10, line 28 and insert in their place the following paragraphs:

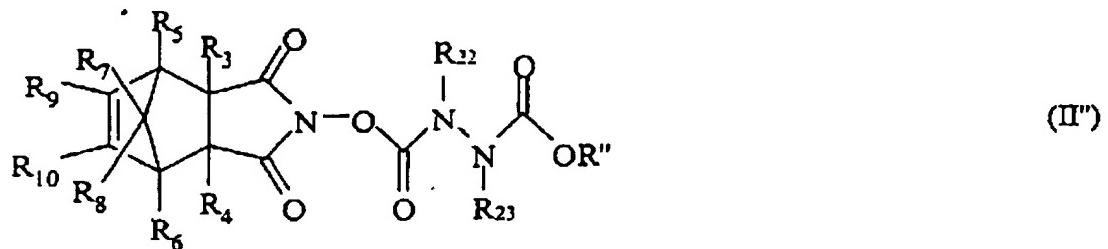
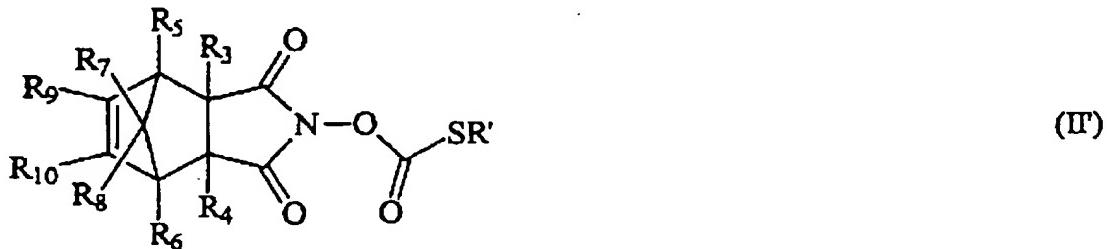
--In another embodiment of the process according to a preferred aspect of the invention, which has already been described above, the polymer having at least one functional group is reacted with an activated derivatizing reagent, the latter being obtained from the reaction of an activating reagent with the derivatizing reagent.

Preferably, activated derivatives of amines, alcohols, thiols, carboxylic acids, sulphonic acids, sulphates, phosphates or phosphonic acids are reacted in the process according to a preferred aspect of the invention with the polymer having at least one functional group, where, in turn in a preferred embodiment, the compounds are activated using ONB-Cl.--

Please delete the paragraph beginning on page 12, line 9 and ending on page 12, line 23 and insert in its place the following paragraph:

--A preferred aspect of the present invention therefore also describes a derivative of an activating reagent according to structure (II), characterized in that it has one of the two structures (II') or (II'')

A18



where R₃ to R₁₀ are as defined above, R₂₂ and R₂₃ are defined as R₁₄ to R₂₀ and can be identical to or different from one another, and R' and R'' can be identical or different and can be alkyl, aryl or aralkyl radicals and are selected in the process according to the invention such that the reaction with the polymer having at least one functional group can be carried out in homogeneous phase. Further, the above substituents on the structures (II') and (II'') are also selected such that the desired interactions with the substrate can be achieved.--

Please delete the paragraphs beginning on page 13, line 7 and ending on page 13, line 21 and insert in their place the following paragraphs:

--In the context of a preferred aspect of the present invention, such polyfunctional derivatizing reagents can be partially or completely activated selectively with an activating reagent and reacted with the polymer having at least one functional group.

A19

The reaction of the polymer having at least one functional group with an activated, polyfunctional derivatizing reagent can be used in the process according to a preferred aspect of the invention for polymer crosslinking, for polymer stabilization and for polymer branching.

A19

Both the reaction of the polymer having at least one functional group with an activated derivatizing reagent and the reaction of the polymer having at least one functional group with an activating reagent and subsequent reaction of the product with a derivatizing reagent by the process according to a preferred aspect of the invention makes it possible to prepare polymer derivatives which have very different spatial arrangements and accordingly can be used for a large number of applications in which the spatial arrangement is of crucial importance.--

P O R T F O R M A T I O N

Please delete the paragraphs beginning on page 13, line 33 and ending on page 14, line 2 and insert in their place the following paragraphs:

--The pH which can be chosen in the reactions is in this case in general in the range from 4 to 14 in the process according to a preferred aspect of the invention, preferably in the range from 5 to 12 and particularly preferably in the range from 5 to 10. For the establishment of a certain pH range, it is possible to work with suitable buffer solutions.

A20

By means of the groups introduced into the polymer in the process according to a preferred aspect of the invention via the derivatization, suitable chemical substances, so-called substrates, can be selectively or specifically bound. The groups introduced act here as receptor groups; the derivatized polymer thus very generally also acts as a receptor.--

Please delete the paragraphs beginning on page 14, line 14 and ending on page 14, line 25 and insert in their place the following paragraphs:

--The interaction or the interactions between the derivatized polymer and the substrate can be formed here in the solid state, in solution, in liquid phase and in the gas phase.

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A21
By means of the process according to a preferred aspect of a preferred aspect of the invention, it is possible to "design" the receptor-substrate interaction using made-to-measure receptor groups. This means that when using the derivatized polymer in, for example, membrane processes, catalysis, filtration or chromatography in the presence of two or more substrates, a selectivity of the interaction with respect to one substrate can be achieved.

In the context of a preferred aspect of the present invention, the degree of derivatization which, in the case in which the derivatized polymer is employed as a receptor, corresponds to the receptor group density, can be influenced such that the best possible interaction with the substrate is achieved and an adequate solubility of the polymer derivative is obtained.--

Please delete the paragraph beginning on page 14, line 31 and ending on page 14, line 35 and insert in its place the following paragraph:

A22
--Accordingly, a preferred aspect of the present invention relates to a derivative of a polymer having at least three functional groups, where at least two of the functional groups are derivatized in such a way that they interact with a suitable substrate as receptor groups and at least one functional group having non-substrate-specific action lies between two of these derivatized groups.--

Please delete the paragraph beginning on page 15, line 34 and ending on page 15, line 36 and insert in its place the following paragraph:

A23
--Accordingly, a preferred aspect of the present invention also describes a derivative of a polymer having at least three functional groups, where at least one functional group not having a substrate specific action is derivatized with an end-capping group.--

Please delete the paragraph beginning on page 16, line 32 and ending on page 16, line 34 and insert in its place the following paragraph:

A24

--A preferred aspect of the present invention further describes a derivative of the type in question here, which has at least one receptor group which has a binding unit which is decisive for the binding of a biological substrate.--

Please delete the paragraph beginning on page 17, line 19 and ending on page 17, line 21 and insert in its place the following paragraph:

--Accordingly, a preferred aspect of the present invention also describes a derivative of a polymer having at least three functional groups, as described above, characterized in that at least one receptor group is an amino acid residue or an amino acid derivative residue.--

A25

Please delete the paragraph beginning on page 18, line 21 and ending on page 18, line 25 and insert in its place the following paragraph:

--Instead of the amino acid, the use of one or more di- or oligopeptides is also possible, where in particular homopeptides, which are only synthesized from identical amino acids, may be mentioned. An example of a dipeptide which may be mentioned is hippuric acid. It is further also possible to use β -, γ - or other structurally isomeric amino acids and peptides derived therefrom such as depsipeptides.--

A26

Please delete the paragraph beginning on page 18, line 30 and ending on page 18, line 32 and insert in its place the following paragraph:

A27

--Accordingly, a preferred aspect of the present invention also describes a derivative of a polymer having at least three functional groups, as described above, which has at least two different receptor groups.--

A28

Please delete the paragraph beginning on page 19, line 4 and ending on page 19, line 6 and insert in its place the following paragraph:

--Accordingly, a preferred aspect of the present invention also describes a process, such as described above, further comprising the step (iii) the derivative of the polymer

A28

having at least one functional group is deformed in the presence of a template compound.--

Please delete the paragraph beginning on page 19, line 13 and ending on page 19, line 15 and insert in its place the following paragraph:

A29

--A preferred aspect of the present invention likewise describes a derivative of a polymer having at least one functional group, characterized in that it has one or more conformations which is/are adapted to a suitable substrate.--

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Please delete the paragraph beginning on page 19, line 29 and ending on page 19, line 31 and insert in its place the following paragraph:

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--A preferred aspect of the present invention therefore also describes a process, as described above, characterized in that a conformation resulting from the deformation of the derivative of the polymer having at least one functional group is fixed.--

A31

Please delete the paragraph beginning on page 20, line 35 and ending on page 20, line 37 and insert in its place the following paragraph:

--Accordingly, a preferred aspect of the present invention also describes a process, as described above, which is characterized in that the conformation resulting from the deformation is fixed by crosslinking.--

A32

Please delete the paragraph beginning on page 23, line 4 and ending on page 23, line 15 and insert in its place the following paragraph:

--The fixed polymer derivatives which can be prepared by the process according to the intervention are used, inter alia, in chromatography. The derivatizing reagents and the conditions for fixing the conformation, as described above, are chosen here such that in the chromatogram the possible substrate elutes at a higher k' value than before the polymer deformation, preferably at the highest k' value of all in the mixture of substances present. The k' values of the impurities in these cases remain approximately identical or are modified in the manner that the quotient $\alpha = k_2' / k_1'$ (k_2'

A32

relates here to the target substance, k_1' to an impurity) is greater than it was before the deformation. Accordingly, it is possible in continuous chromatography, in particular in SMB chromatography, to reduce a multi-substance separation problem to a two-substance separation problem, since the product, i.e. the possible substrate, goes into the extract, and all by-products together go into the raffinate.--

Please delete the paragraphs beginning on page 23, line 21 and ending on page 24, line 27 and insert in their place the following paragraph:

A33

--In a further preferred embodiment, a preferred aspect of the present invention describes a derivative of a polymer having at least one functional group, which acts as a receptor for the binding of at least one substrate via non-covalent receptor-substrate interaction, where the binding of the at least one substrate can take place via at least two, preferably three, identical or different types of interactions on account of the chemical constitution of the receptor, these multiple interactions in general being synergistically reinforced, e.g. by polyvalent enthalpy gain.--

Please delete the paragraphs beginning on page 23, line 37 and ending on page 24, line 26 and insert in their place the following paragraphs:

A34

--A preferred aspect of the present invention therefore likewise relates to a process for the binding of at least one substrate to at least one receptor group via non-covalent receptor-substrate interaction, wherein the compound employed having at least one receptor group is a derivative of a polymer having at least one functional group, prepared by a process as described above, or a derivative as defined above.

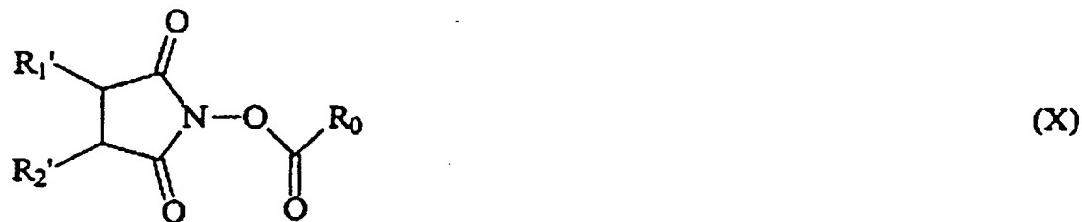
In addition, a preferred aspect of the present invention also describes a process, as described above, where the process is a chromatography process, in particular an SMB process, a filtration process, a separation process by means of one or more membranes or a catalytic process.

According to a preferred aspect of the invention, the activating reagents employed are compounds of the general structure (I), as described above, where the radicals R_1 and

R_2 are selected such that the reaction with the polymer having at least one functional group can proceed in homogeneous phase.

A preferred aspect of the present invention therefore relates to a compound of the general structure (X)

A34



wherein R_0 is a halogen atom or a radical (X')



and R_1' , R_2' ; R_1'' and R_2'' are identical or different and are hydrogen, straight-chain or branched-chain alkyl, aryl, cycloalkyl, heterocyclic or aralkyl radicals having up to 30 C atoms, or either R_1' and R_2' or R_1'' and R_2'' or both R_1' and R_2' and R_1'' and R_2'' are linked to at least one carbocycle or to at least one heterocycle or to at least one carbocycle and to at least one heterocycle, compounds of the following structures (X_1) to (X_7) being excluded:--

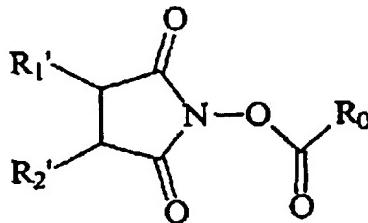
Please delete the paragraph beginning on page 26, line 1 and ending on page 26, line 3 and insert in its place the following paragraph:

A35
--Furthermore, a preferred aspect of the present invention also describes a compound, such as described above, which is characterized in that it is selected from the group consisting of the compounds comprising the following structures (X₈) to (X₃₉):--

Please delete the paragraphs beginning on page 32, line 6 and ending on page 32, line 22 and insert in its place the following paragraphs:

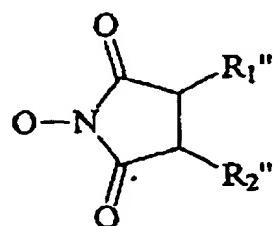
--A preferred aspect of the present invention therefore also describes the use of a compound of the general structure (X)

A36



(X)

wherein R₀ is a halogen atom or a radical of the structure (X')



(X')

and R₁', R₂', R₁'' and R₂'' are identical or different and are hydrogen, straight-chain or branched-chain alkyl, aryl, cycloalkyl, heterocyclic or aralkyl radicals having up to 30 C atoms or either R₁' and R₂' or R₁'' and R₂'' or both R₁' and R₂' and R₁'' and R₂'' are linked to at least one carbocycle or to at least one heterocycle or to at least one carbocycle and to at least one heterocycle, for the activation of at least one functional group of at least one further compound.

A36

A preferred aspect of the present invention is illustrated in greater detail below with the aid of some examples.--

Please delete the paragraph beginning on page 34, line 9 and ending on page 34, line 19 and insert in its place the following paragraphs:

--12.56g (135 mmol) of poly(allylamine hydrochloride) were dissolved in 250 ml of water and the pH was adjusted to 5 using 10% strength aqueous NaHCO₃ solution. A solution of 2.96 g (9.45 mmol) of N-(benzyloxycarbonyloxy)-5-norbornene-2,3-dicarboximide in 45 ml of DMSO was added dropwise at 20°C in the course of 30 mm. The reaction mixture was then stirred at 20°C for 24 h. The pH was kept at a value of 5 during the reaction time by addition of 10% strength aqueous NaHCO₃ solution. 200 ml of 10% strength aqueous NaHCO₃ solution were added to the clear reaction mixture. The reaction mixture was then introduced dropwise into 1000 ml of methanol. The derivatized polymer quantitatively precipitated was filtered off through a cellulose nitrate filter (8 µm) and dried in a high vacuum for 24 h. The degree of derivatization of 7% was confirmed by means of ¹H-NMR spectroscopy.--

A37

Please delete the paragraph beginning on page 34, line 24 and ending on page 34, line 33 and insert in its place the following paragraph:

--12.56g (135 mmol) of poly(allylamine hydrochloride) were dissolved in 250 ml of water and the pH was adjusted to 5 using 10% strength aqueous NaHCO₃ solution. A solution of 5.92 g (18.9 mmol) of N-(benzyloxycarbonyloxy)-5-norbornene-2,3-dicarboximide in 55 ml of DMSO was added dropwise at 20°C in the course of 30

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A38

min. The reaction mixture was then stirred at 20°C for 24 h. The pH was kept at a value of 5 during the reaction time by addition of 10% strength aqueous NaHCO₃ solution. The reaction mixture was added dropwise in 600 ml of 10% strength aqueous NaHCO₃ solution. The derivatized polymer quantitatively precipitated here was filtered off through a cellulose nitrate filter (8 µm) and dried in a high vacuum for 24 h. The degree of derivatization of 14% was confirmed by means of ¹H-NMR spectroscopy.--

Please delete the paragraph beginning on page 34, line 38 and ending on page 35, line 8 and insert in its place the following paragraph:

--13.95g (150 mmol) of poly(allylamine hydrochloride) were dissolved in 200 ml of water and the pH was adjusted to 5 using 10% strength aqueous NaHCO₃ solution. A solution of 9.39g (30 mmol) of N-(benzyloxycarbonyloxy)-5-norbornene-2,3-dicarboximide in 50 ml of DMSO was added dropwise at 20°C in the course of 30 min. The reaction mixture was then stirred at 20°C for 24 h. The pH was kept at a value of 5 during the reaction time by addition of 10% strength aqueous NaHCO₃ solution. The reaction mixture was added dropwise in 500 ml of 10% strength aqueous NaHCO₃ solution. The derivatized polymer quantitatively precipitated here was filtered off through a cellulose nitrate filter (8 µm) subsequently washed with water and dried in a high vacuum for 24 h. The degree of derivatization of 20% was confirmed by means of ¹H-NMR spectroscopy.--

A39

Please delete the paragraph beginning on page 37, line 27 and ending on page 37, line 31 and insert in its place the following paragraph:

--Silica gel 300 Å, 20 µm (Daisogel SP 300-15/30), coated with 3 layers of poly(benzyl N-allylcarbamate) having a degree of derivatization of 7%, which are crosslinked to 2% with dodecanedioic acid bis(N-hydroxy-5-norbornene-2,3-dicarboximide) ester = (1),

succinic acid bis(N-hydroxy-5-norbornene-2,3-diacarboximide) ester = (2)--

Please delete the paragraph beginning on page 38, line 1 and ending on page 38, line 5 and insert in its place the following paragraph:

A41
--A column packed with (1) was conditioned with 0.2% strength (10.5 mmol/l) 5-methyl-5-phenylhydantoin solution (substrate) in CHCl₃ and a flow of 0.6 ml/min, about 40 mg of the substrate being absorbed on the column 80 µl of glacial acetic acid were then injected and the outflow was collected in two fractions:--

Please delete the heading "Patent Claims" and insert in its place the heading --
What is claimed is:--

In the Claims:

Please cancel claims 7 and 8 without disclaimer or prejudice.

Please amend the remaining claims as follows:

Sbj
A42
1. (Amended) A process for the preparation of a derivative of a polymer having at least one functional group, wherein the process comprises:

(i) reacting the polymer having at least one functional group, with at least one activating reagent or at least one derivative of an activating reagent in a homogeneous phase.

2. (Amended) The process according to Claim 1, further comprising:

(ii) reacting the reaction product from the polymer having at least one functional group and the activating reagent, with a derivatizing reagent.

3. (Amended) The process according to Claim 1, wherein at least one derivative of the activating reagent is obtained by prior reaction of the activating reagent with a derivatizing reagent.